AMENDMENTS TO THE SPECIFICATION

On pages 21 and 22, please replace paragraphs [0078] and [0079] with the following:

[0078] GP88 is also a tumor inducing factor in human cancers. As seen in the 1246-3A cell line, a loss of responsiveness to insulin (or to IGF-I) and a concurrent increase in malignancy has been well documented (13, 14) in several human cancers including but not limited to breast cancers. Specifically, breast carcinoma is accompanied by the acquisition of an insulin/IGF-I autocrine loop, which is also the starting point of the development of tumorigenic properties in the mouse model system discussed above. Furthermore, GP88 expression is elevated in human breast carcinomas. More specifically, with reference to FIG. 5, human GP88 was highly expressed in estrogen receptor positive and also in estrogen receptor negative insulin/IGF-I independent highly malignant cells. Also, GP88 is a potent growth factor for mammary epithelial cells (FIG. 6). The data in FIG. 5 was obtained by cultivating MCF7, MDA-MB-453 and MDA-MB-468 cells in DME/F12 medium supplemented with 10% fetal bovine serum (FBS). RNA was extracted from each cell line by the ~~RNAzol~~RNAZOL method and poly-A^+ RNA prepared. GP88 mRNA expression was examined by Northern blot analysis with 3 μg of poly-A^+ RNA for each cell line using a ^{32} P-labeled GP88 cDNA probe.

[0079] For Northern blot analysis of GP88 mRNA expression in rodent cells or tissues (mouse and rats), we used a mouse GP88 cDNA probe 311 bp in length starting at nucleotide 551 to 862 (corresponding to amino-acid sequence 160 to 270). RNA can be extracted by a variety of methods (Sambrook , Molecular Biology manual: 35) well known to people of ordinary skill in the art. The method of choice was to extract RNA using ~~RNAzol~~RNAZOL (Cinnabiotech) or ~~Trizol~~TRIZOL (Gibco-BRL) solutions which

consists of a single step extraction by guanidinium isothiocyanate and phenol - chloroform.

On pages 34-35, please replace paragraph [0118] with the following:

[0118] Phosphorothioate antisense oligonucleotides may be used (39). Modifications of the phosphodiester linkage as well as of the heterocycle or the sugar may provide an increase in efficiency. With respect to modification of the phosphodiester linkage, ~~phophorothioate~~ phosphorothioate may be used. An N3'-P5' phosphoramidate linkage has been described as stabilizing oligonucleotides to nucleases and increasing the binding to RNA (40). Peptide nucleic acid (PNA) linkage is a complete replacement of the ribose and phosphodiester backbone and is stable to nucleases, increases the binding affinity to RNA, and does not allow cleavage by RNAse H. Its basic structure is also amenable to modifications that may allow its optimization as an antisense component. With respect to modifications of the heterocycle, certain heterocycle modifications have proven to augment antisense effects without interfering with RNAse H activity. An example of such modification is C-5 thiazole modification. Finally, modification of the sugar may also be considered. 2'-O-propyl and 2'-methoxyethoxy ribose modifications stabilize oligonucleotides to nucleases in cell culture and in vivo. Cell culture and in vivo tumor experiments using these types of oligonucleotides targeted to c-raf-1 resulted in enhanced potency. As general references for antisense oligonucleotides, see (32-34)

On pages 45 and 46, please replace paragraphs [0144] and [0145] with the following:

[0144] Total cellular RNA was isolated by ~~RNAzol~~RNAZOL solution (Cinnabiotech) or ~~Trizol~~TRIZOL solution (Life Technologies) based on a modification of the single step guanidinium isothiocyanante/phenol chloroform method (52).

[0145] Fifteen or twenty micrograms of total RNA per sample were subjected to electrophoresis on a denaturing 1.2% agarose gel containing 0.22 M formaldehyde in 1x MOPS (10x MOPS: 0.2 M MOPS, 50 mM NaOAc 10 mM EDTA). RNA was blotted on nitrocellulose membrane (MSI Inc., Westboro, MA) by overnight capillary transfer in 10x SSC (20x SSC = 3M NaCl, 0.3M Na Citrate pH 7.0). The filters were baked at 80ºC under vacuum for 2 hrs and then prehybridized at 42ºC for 4 hrs in hybridization solution consisting of 50% formamide, 5 X SSPE (1 X SSPE = 0.16 M sodium chloride, 50 mM sodium phosphate pH 7.4, 1 mM EDTA), 1% SDS, 5 X Denhardt's solution (1X Denhardt's solution = 0.02 % each of polyvinylpirrolidone, Ficoll and bovine serum albumin), 1 μg/ml poly-A and 100 μg/ml denatured salmon sperm DNA at 42ºC. Hybridization was performed overnight at 42ºC in the same solution with 10^6cpm/ml of random-primed ^{32}P-labeled GP88 cDNA probe. Filters were washed twice for 25 min at 42ºC in 2 X SSC and 1% SDS, followed by two 15 min. washes at 56ºC in 0.2 X SSC and 1% SDS. Dried filters were exposed to ~~Kodak~~KODAK XAR-5 film (Kodak, Rochester, NY) at -70ºC with an intensifying screen (Dupont, Boston, MA). Results were quantitated by densitometric scanning. Ribosomal protein L_{32} mRNA was detected as internal standard for normalizing RNA loading.